

IN THE SPECIFICATION

Please replace paragraph [0041] with the following paragraph:

[00158] As used herein, “significant” expression, or a marker “significantly” expressed is intended to refer to differential expression of a predictive marker which is indicative of responsiveness or non-responsiveness. A marker or marker set in a patient is “significantly” expressed at a higher (or lower) level than the normal level of expression of a marker or marker set if the level of expression of the marker or marker set is greater or less, respectively, than the normal level by an amount greater than the standard error of the assay employed to assess expression[.,]. Preferably a significant expression level is at least twice, and more preferably three, four, five or ten times that amount. Alternately, expression of the marker or marker set in the patient can be considered “significantly” higher or lower than the normal level of expression if the level of expression is at least about two, and preferably at least about three, four, or five times, higher or lower, respectively, than the normal level of expression of the marker or marker set. Still further, a “significant” expression level may refer to level which either meets or is above or below a pre-determined score for a predictive marker set as determined by methods provided herein.

Please replace paragraph [0050] with the following paragraph:

[0050] Table 1 lists markers identified using statistical analysis applied to genes from 44 myeloma patient samples. The markers in Table 1 are significantly expressed in samples from patients that are either responsive or non-responsive to treatment with the proteasome inhibitor bortezomib. Thus, one would appreciate that the markers identified can function in a predictive model to prospectively identify patients’ response to proteasome inhibition therapy, including response to bortezomib or other proteasome inhibition therapies known in the art as well as those described in further detail herein. In particular, the markers in Table 1 are correlated with a positive response to therapy (referred to herein as “~~non-predictive~~ responsive markers, (NR R)”). A patient with a positive response (either complete, partial or minimal; see Table C) to therapy is hereinafter referred to as a “responder”. Additionally, the predictive markers in Table 1 are correlated with a negative or poor response to an agent (referred to herein as “non-predictive markers, (NR)”). A patient with a poor response (called a progressive or refractory disease; see

Table C) to treatment is hereinafter referred to as a “non-responder”. A patient with no response to treatment is hereinafter referred to as “stable” (see Table C).

Please replace paragraph [0056] with the following paragraph:

[0056] Table 1 identifies markers whose expression correlates with responsiveness to a proteasome inhibitor. It is preferable to determine the expression of at least one, two or more of the identified predictive markers; or three or more of the identified predictive markers comprising a set of the identified predictive markers.[[.]] Thus, it is preferable to assess the expression of a set or panel of predictive markers, *i.e.*, the expression profile of a predictive marker set.

Please replace paragraph [00158] with the following paragraph:

[00158] The determination of percent identity between two sequences can be accomplished using a mathematical algorithm determining the number of identical positions shared between two sequences. Determination can be carried out using any known method in the art for comparison of identity and similarity. Examples of methods used can include for example, a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin and Altschul (1990) *Proc. Natl. Acad. Sci. USA* 87:2264-2268, modified as in Karlin and Altschul (1993) *Proc. Natl. Acad. Sci. USA* 90:5873-5877. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-410. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to a nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to a protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.* (1997) *Nucleic Acids Res.* 25:3389-3402. Alternatively, PSI-Blast can be used to perform an iterated search which detects distant relationships between molecules. When utilizing BLAST, Gapped BLAST, and PSI-Blast programs, the default parameters of the respective programs (*e.g.*, XBLAST and NBLAST) can be used.—See <http://www.ncbi.nlm.nih.gov> (accessible at the website maintained by National Center for Biotechnology Information, Bethesda, MD, USA). Another example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller, (1988)

CABIOS 4:11-17. Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used. Yet another useful algorithm for identifying regions of local sequence similarity and alignment is the FASTA algorithm as described in Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85:2444-2448. When using the FASTA algorithm for comparing nucleotide or amino acid sequences, a PAM120 weight residue table can, for example, be used with a k -tuple value of 2. The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating percent identity, only exact matches are counted.

Please replace paragraph [00220] with the following paragraph:

[00220] A set of one or more gene transcripts that together classify samples into sensitive and resistant groups (or responsive and non-responsive), in the context of a particular classifier algorithm, is referred to as a “model.” The gene transcripts are referred to as “features.” Determining which combination of gene transcript(s) best classifies samples into sensitive and resistant groups is referred to as “model selection.” The following section describes the process of how the models of the present invention were identified. Exemplary models are set forth in Table 4, Table 5, and Table 6. The methods provided herein along with the single marker identification or Predictive markers can be used to identify additional models comprising markers of the invention.

Please replace paragraph [00249] with the following paragraph:

[00249] Here we illustrate how to apply a Weighted Voting model to obtain a prediction of Response or Non-response for a given patient, using the algorithm described herein. Using the 44 patients classified into Responsive or Nonresponsive groups, ~~the table below~~ Table 5 shows the SNR scores and decision boundaries for each of the markers in a Weighted Voting predictive set built from the data set. Also indicated is whether the marker is more highly expressed in Responsive (R) or in Non-responsive (NR) patients. For one illustrative Non-responsive patient in the data set, the votes contributed by each marker are shown in Table 5. The sum of the vote weights is less than 0, indicating a prediction of Non-responsive. The confidence in the predicted class (Non-responsive) is 0.8431.